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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/519,677	01/07/2005	Akira Yanagawa	264232US0PCT	9965

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EXAMINER
ALSTRUM ACEVEDO, JAMES HENRY

ART UNIT	PAPER NUMBER
1616	

NOTIFICATION DATE	DELIVERY MODE
12/19/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/519,677	YANAGAWA, AKIRA	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/4/07*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 11-20 are pending. Applicant previously cancelled claims 1-10 and claims 21-22. Receipt and consideration of Applicant's amended claim set and remarks/arguments submitted on October 4, 2007 are acknowledged.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/4/07 has been entered.

Moot Rejections/objections

All rejections and/or objections of claims 1-10 cited in the previous office action mailed on June 15, 2006 **are moot**, because said claims have been cancelled.

Previous Rejections of Record

All the outstanding rejections of record are withdrawn, per Applicants claim amendments limiting the opioid analgesics to opioids that lack sedating effects. New rejections are made as set forth below in the instant office action.

Specification

The objection to the abstract because it consists of more than one paragraph **is maintained** for the reasons of record set forth on page 2 of the previous office action mailed on June 15, 2006. An amended abstract was not received with Applicants' response dated November 8, 2006.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Applicant Claims
2. Determining the scope and contents of the prior art.
3. Ascertaining the differences between the prior art and the claims at issue, and resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out

the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 11-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yanagawa (U.S. Patent No. 5,603,943) ("USPN '943") in view of Wermeling (US 2003/0077300) and the 1999-2000 Drug Information Handbook ("DIH") (Lacy, C. F.; Armstrong, L.L.; Goldman, M. P.; Lance, L. L., Lexi-Comp, Inc: Hudson, OH, 1999, pp 349-350 and 414-417).

Applicant Claims

Applicant claims (1) a composition for nasal absorption comprising a carrier of calcium carbonate and/or calcium phosphate having an average particle size less of 20-100 microns an effective dose of an opioid analgesic selected from the group consisting of fentanyl, fentanyl citrate, and a droperidol/fentanyl citrate preparation and (2) a method of treating post surgery or cancer pain comprising intranasally administering said composition.

Determination of the Scope and Content of the Prior Art (MPEP §2141.01)

The teachings of Yanagawa were set forth on pages 4-5 of the office action mailed on June 15, 2006. Additional relevant teachings are set forth herein. Yanagawa teaches that the physiologically acceptable substances that may be used with the nasally administrable inorganic carriers may be any that has a molecular weight less than 40,000 such as those that are employed as ordinary pharmaceuticals, for example, **antiemetics** (col. 4, lines 28-44)

DIH teaches that **droperidol is a known antiemetic (i.e. anti-nausea drug)** (pp 349). DIH teaches that **fentanyl and fentanyl citrate are known opioid analgesics that *may cause nausea*** and other side effects (pp 414). DIH teaches that **the preparation of droperidol/fentanyl is known** and sold under the trademark name of INNOVAR® (pp 350).

Wermeling teaches a system and method for **intranasal administration of opioids, including fentanyl** (title; abstract; [0022]; [0129]; claims 15 and 20). Wermeling's formulations are in the form of liquids [0129].

Ascertainment of the Difference Between Scope the Prior Art and the Claims (MPEP §2141.012)

Yanagawa lacks the express teaching of compositions wherein the active substance is selected from the group consisting of fentanyl, fentanyl citrate, or a droperidol/fentanyl citrate preparation. This deficiency is cured by the teachings of the DIH. Wermeling is provided as a supporting reference to demonstrate that the nasal delivery of opioids was known at the time of the instant invention.

Finding of Prima Facie Obviousness Rational and Motivation (MPEP §2142-2143)

It would have been prima facie obvious to a person of ordinary skill in the art to utilize and opioid analgesic as the active substance in Yanagawa's compositions, because Yanagawa teaches that suitable active substances are those with a molecular weight below 40,000 that are employed as ordinary pharmaceuticals. It is clearly evident from the teachings of the DIH, that fentanyl; opioid analgesics in general, are ordinarily employed as pharmaceuticals. Thus, an

ordinary skilled artisan would have been motivated to utilize an opioid analgesic in Yanagawa's compositions. At the very least, the incorporation of a conventional opioid analgesic into Yanagawa's compositions would have been obvious to try, because opioids are ordinarily employed pharmaceuticals; are known to be nasally administrable (Wermeling), and thus the ordinary skilled artisan would have a reasonable expectation of predictably and successfully administering an opioid analgesic (e.g. fentanyl) using Yanagawa's modified composition. Regarding the combination of droperidol/fentanyl citrate, this would have been obvious because fentanyl is known to cause nausea as one of its side effects and droperidol is a well-known antiemetic, which is commercially sold in combination with fentanyl under the trademark of INNOVAR®. An ordinary skilled artisan would have had a reasonable expectation of success upon modification of the teachings of Yanagawa to utilize an opioid analgesic, selected from fentanyl, fentanyl citrate, or a droperidol/fentanyl citrate preparation; because it is well known that opioids are nasally administrable (Wermeling). Furthermore, fentanyl, fentanyl citrate, and droperidol all meet the indicated molecular weight requirement taught by Yanagawa and all these drugs are also ordinarily employed as pharmaceuticals. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Response to Arguments

Applicant's arguments filed October 4, 2007, as these may apply to this new rejection, have been fully considered but they are not persuasive. Applicant's traversal based on the

assertion that (1) Yanagawa allegedly does not describe or suggest fentanyl, fentanyl citrate, or a droperidol/fentanyl citrate preparation; (2) peptides are taught by Yanagawa as being the preferred active substance; (3) Yanagawa is allegedly not enabled for physiologically active substances other than peptides and thus is allegedly not a proper reference alone or combined with the DIH.

The Examiner respectfully disagrees. Concerning argument (1), in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). By attacking the teachings of Yanagawa without considering the **combined teachings of Yanagawa and the DIH**, the Applicant cannot demonstrate nonobviousness. Regarding (2), it is accepted that a reference's indicated preferences are not considered to limit the teachings of a given reference or constitute a teaching away. Regarding (3), Applicant has provided no technical or scientific basis as to why an ordinary skilled artisan would not be enabled to make Yanagawa's invented compositions modified to utilize fentanyl, fentanyl citrate, or a droperidol/fentanyl citrate as the physiologically active substance or to use said compositions to nasally administer an opiate. It is noted that at the time of Applicant's claimed invention it was well known that opioids could be administered nasally. Yanagawa's claims also recite many non-peptide active substances as being suitable. Furthermore, Applicant is reminded that an issued U.S. patent has a presumption of validity and enablement, and that the claims of an issued U.S. patent are considered fully enabled embodiments. Thus, mere argument in the absence of objective evidence that Yanagawa is not enabled to make nasally administrable

compositions comprising (i) a carrier of calcium carbonate and/or calcium phosphate having an average particle size less of 20-100 microns and (ii) an effective dose of an opioid analgesic selected from the group consisting of fentanyl, fentanyl citrate, and a droperidol/fentanyl citrate preparation is unpersuasive. Therefore, the claimed invention, as a whole, would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, because the combined teachings of the prior art is fairly suggestive of the claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 11-20 are rejected as being unpatentable over claims 1-2, 4, and 9-14 of U.S. Patent No. 5,603,943 (USPN '943) in view of Wermeling (US 2003/0077300) and the 1999-2000 Drug Information Handbook ("DIH") (Lacy, C. F.; Armstrong, L.L.; Goldman, M.

P.; Lance, L. L., Lexi-Comp, Inc: Hudson, OH, 1999, pp 349-350 and 414-417) for the reasons of record set forth on pages 7-8 of the office action mailed on June 15, 2006 and set forth above in the instant office action. Applicant's claims have been described above as have the teachings of the DIH and Wermeling. The claims of Yanagawa were described in the office action mailed on June 15, 2006. The difference between Applicant's claims and those of Yanagawa is that the claims of USPN '943 do not recite compositions comprising fentanyl, fentanyl citrate, or a droperidol/fentanyl citrate preparation as the physiologically active substance. This deficiency is cured by the teachings of Wermeling and the DIH, set forth above in the instant office action. Therefore, a person of ordinary skill in the art at the time of the instant invention would have found claims 11-20 *prima facie* obvious over claims 1-2, 4, and 9-14 of U.S. Patent No. 5,603,943 (USPN '943) in view of Wermeling (US 2003/0077300) and the 1999-2000 Drug Information Handbook ("DIH") (Lacy, C. F.; Armstrong, L.L.; Goldman, M. P.; Lance, L. L., Lexi-Comp, Inc: Hudson, OH, 1999, pp 349-350 and 414-417).

Conclusion

Claims 11-20 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-6:30, with every other Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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